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(54) Title: FUSION RECEPTORS SPECIFIC FOR PROSTATE-SPECIFIC MEMBRANE ANTIGEN AND USES THEREOF

(57) Abstract

A fusion receptor composition which is effective to promote a cellular immune response to prostate-specific membrane antigen (PSMA) *in vivo* when the fusion receptors is expressed by T lymphocytes has the structure: PSMA-scFv: connector: cytoplasmic domain. The PSMA-scFv in this structure is a single chain antibody cloned from the V region genes of a hybridoma specific for PSMA. The connector region is provided to give a spacing between the OSMA-scFv and the cytoplasmic domain, such that both can retain substantial function. A suitable connector is the CD8 hinge, although other connectors of greater or lesser length might be used. The cytoplasmic domain is included to direct the function of the fusion receptor. One exemplary cytoplasmic domain which can be used in the fusion receptor of the invention is a T cell receptor ζ-chain cytoplasmic domain. An expression vector encoding the fusion receptor is transduced into primary T lymphocytes obtained from an individual to be treated. The transduced lymphocytes are returned to the patient where cells expressing the fusion receptor secrete interleukin 2 and proliferate in response to PSMA-positive cells. The resulting cytotoxic lymphocytes specifically lyse cells expressing PSMA and thus can be used to target PSMA-positive tumor cells and neovasculature.

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